Amendments to the Specification

Please amend the sub-heading beginning on page 1, before the title of the invention as follows:

~~Description~~

Please insert before line 5, on page 1 of the specification the following heading:

BACKGROUND OF THE INVENTION

Please amend the sub-heading beginning on page 1, line 10, as follows:

~~Technical Field~~

1. Technical Field

Please amend the sub-heading beginning on page 1, line 10, as follows:

~~Background of the Invention~~

2. Description of Related Art

Please amend the heading beginning on page 2, line 26, as follows:

~~Disclosure of the Invention~~

SUMMARY OF THE INVENTION

Please amend the paragraph beginning on page 3, line 4, as follows:

However, since during research directed towards achieving these objects the following problems were found to exist, the present invention has the additional ~~the~~ object of solving these problems.

Please amend the paragraph beginning on page 3, line 12, as follows:

Specifically, since many cells cannot survive or proliferate unless adhering to a scaffold, the cells adhere to the wall of the culture vessel, using it as a scaffold. Hence, when the cells are to be transplanted into a living body, the cells adhering to surfaces in the vessel must be detached. To do this, operations including physical detachment and detachment using a chemical agent such as trypsin and/or EDTA can be used, but these operations can adversely affect the cells. Furthermore, these types of cell operations are difficult to implement for anyone not ~~in~~ trained in advanced techniques and not in possession of a well-equipped facility.

Please amend the paragraph beginning on page 6, line 25, as follows:

In the case of a cell handling device of the syringe-type, it is desirable to form a gas permeable region across all or a portion of the main body part storing the cells and across a portion of the plunger. Since when a gas permeable region is formed across a portion of the main body it will have a limited area, designing a device in which a material with a comparatively high permeability is used so that sufficient gas for the survival of the cells can be secured is considered to be desirable. Note that the degree of permeability will depend on the minimum gas concentration (oxygen, carbon dioxide) needed for the survival of the cells. In other words, though the amount of gas needed for the survival of the cells is different according to the type of cells, in order to have the cells survive, it is preferable that a material with a high permeability is used and that a sufficient level of gas exchange takes place.

Please amend the paragraph beginning on page 7, line 17, as follows:

One material with superior gas permeability, which is used when the gas permeable region is provided across a portion of the main body, is porous film. By controlling the diameter of the pores of this porous film, impermeability with respect to liquids can be maintained. On account of this it has been discovered that if a film whose pores are formed to be sufficiently small to guarantee its impermeability with respect to liquids is used, sufficient gas permeability can be ensured, even if only a comparatively small area of the material is provided.

Please amend the paragraph beginning on page 9, line 18, as follows:

Conventionally, cells to be transplanted in a regenerative medical treatment were cultured and stored using, for example, a culture-use petri dish, or the like. However, since, in this type of conventional cell handling device, cells adhered to the internal surfaces, some processing to detach the cells was necessary when transplantation to a living body took place. Further, in order to carry out this detachment processing, a highly skilled and experienced operator working with equipment that strictly prevents contamination was required, and regenerative medical treatment could not be carried out easily. With the cell handling device of the present invention, on the other hand, detachment processing is not required when the cells are removed from the cell handling device, and since cells can be transplanted undamaged to a living body without using either physical detachment methods or drugs, satisfactory implementation of regenerative medical treatments can be anticipated. Further, as carrying out the detachment process is unnecessary and the cells stored in the cell handling device can be transplanted as they are into a living body, the complexity of the transplantation can be reduced and even an operator who ~~has~~ does not have special expertise can easily transplant cells.

Please amend the paragraph beginning on page 10, line 10, as follows:

Moreover, the present inventors pursued research based on their own ideas about the form and material of the scaffold used to have cells proliferate and induce differentiation in cells for regenerative medical treatments, and by the combined actions of setting the shape of the scaffold to ~~a be~~be a grain-like shape and forming the scaffold from a material that is bioabsorbable, they were able to demonstrate a great simplification in the operations associated with cell culture, and this led them to develop the tissue regeneration composition of the present invention. Specifically, the tissue regeneration composition of the present invention includes a fluidity medium and cell scaffold microcarriers, granular in form, which become scaffolds for the cells, the cell scaffold microcarriers being composed of a material that is bioabsorbable, and the cells adhering to the cell scaffold microcarriers.

Please amend the heading beginning on page 13, line 19, as follows:

~~Brief Description of the Drawings~~
BRIEF DESCRIPTION OF THE DRAWINGS

Please amend the heading beginning on page 14, line 13, as follows:

~~Best Mode for Carrying Out the Invention~~
DETAILED DESCRIPTION OF THE INVENTION

Please amend the paragraph beginning on page 16, line 16, as follows:

Here, the cell suspension can be made to include the various type of cells used in regenerative medical treatments. The cells can be any of the various types described above depending on the aim of the treatment. There are no particular limits to the type of cell that can be

used and besides stem cells, differentiated cells or their progenitors can be used. Some examples of stem cells that can be used are ~~embryrionic~~ embryonic stem cells (ES cells), embryonic germ cells (EG cells), adult stem cells (AS cells), mesenchymal stem cells, neural stem cells, endothelial stem cells, hematopoietic stem cells, and hepatic stem cells. Examples of the differentiated cells include bone cells, chondrocytes, muscle cells, heart muscle cells, nerve cells, tendon cells, fat cells, pancreatic cells, heptocytes, liver cells, hair follicle cells, blood cells and the like. Thus, embryonic stem cells and other stem cells at various stages of differentiation, and cells that have differentiated to form various tissues can be used. Of these, when adhering cell types are used, making the cell handling device non-adhesive with respect to cells and using fine grained scaffolds are effective. This is because adhering cells require scaffolds for proliferation and differentiation.

Please amend the paragraph beginning on page 18, line 10, as follows:

FIGs. 1A-1C show the structure of the syringe-type cell handling device 1 of the First Embodiment that is one example of the cell handling device of the present invention. FIG. 1A is a perspective view, FIG. 1B is a side elevation, and FIG. 1C is a cross-section through X-X' of FIG. 1B.

Please amend the paragraph beginning on page 18, line 19, as follows:

The syringe main body 2 is composed of a cylindrical body 3 made by injection molding a material that is non-adhesive with respect to cells to form a cylinder, and a gas permeable film 20 which is described below.

Please amend the paragraph beginning on page 25, line 3, as follows:

Moreover, though the syringe-type cell handling device 1 is capable of gas exchange with the exterior due to the provision of the gas permeable region 21, it is formed so ~~as~~ that bacteria do not invade through the gas permeable region 21 into the syringe main body 2. Thus contamination is

prevented and the cells can be stored satisfactorily. The degree to which contamination is prevented can, as discussed above, be adjusted as appropriate. When a gas permeable material is used as the gas permeable film 20, for example, adjustment is achieved by adjusting the thickness of the material and, when porous film used, by appropriately setting the diameter of the holes, or the like. Note, however, that the degree of permeability required by the cell handling device must be taken into consideration when such adjustment is carried out.

Please amend the paragraph beginning on page 35, line 13, as follows:

In this method concentrated and separated surface marker Leneage negative Scal+sKit+ (hereinafter KSL; suspended cells) of hematopoietic stems cells (HSC) from mouse bone marrow were purified, and in each syringe, 10000 cells were suspended in 2 mL of culture liquid and cultured for three days. Next, ~~The~~ the surface markers and colony assay were used to evaluate the number of surviving HSC.

- The following types of culture liquid were used.
  Stem Span medium (Stemcell Technology)
  50 ng/mL murine stem cell factor (mSCF; Peprotech)
  20 ng/mL human filt-3-liganc (Peprotech)
  20 ng/mL murine thrombopoietin (mTPO; Stemcell Technology)
- Type of antibiotic; 0.05 μg/ml Streptomycin

Please amend the paragraph beginning on page 37, line 19, as follows:

Any of the gas permeable materials described in the First to Fourth Embodiments can be used to construct the cell handling device 200. However, in the Fifth Embodiment, since the cell handling device is largely constructed from the gas permeable material, the cylindrical form of the cell handling device is maintained by the gas permeable material, and it is therefore considered preferable that a gas permeable material of sufficient strength is used. Note also that when a porous

film is used as the material for the cell handling device 200, there are cases in which the transparency of the cell handling device falls, making it harder to check the cell suspension 100 inside. In such cases, the transparency of the cell handling device 200 should be ensured by constructing at least a part thereof (the back end 202 of the main body surrounding walls ~~210~~ 201) from a gas permeable resin, enabling the cell suspension 100 held inside the device to be checked. Such a method can ~~may~~ also be used for a cell handling device 300 of the Sixth Embodiment, which is described below.

Please amend the paragraph beginning on page 38, line 27, as follows:

The superior performance of this kind of cell handling device 200 is also displayed when the device is used in regenerative treatments. By removing the cap 60, attaching a needle or catheter to the leur 203, bringing the device to a predetermined position inside a living body, and simply applying a pressure via the hands or a medical device to the back end 202 of the main body surrounding walls ~~210~~ 201, cells can be injected quickly and easily into the living body while the occurrence of contamination is avoided. Further, when a porous film is used in a part of the device, an operation to remove bubbles from the cell suspension 100 can be efficiently carried out by pressing on the back end 202.

Please amend the paragraph beginning on page 42, line 16, as follows:

The syringe-type cell handling device 1 of the Seventh Embodiment is of a construction in which the cell suspension 100 is held liquid-tight in the bag 50. The principal distinguishing characteristic of the Seventh Embodiment relates to the bag 50. Namely, the bag 50 is constructed from a gas permeable material and is liquid-tight, and consequently, the cells in the cell suspension 100 stored inside the bag 50 do not pass to the exterior except through the leur 51, and gas exchange can take place with the exterior of the bag 50.

Please amend the paragraph beginning on page 49, line 28, as follows:

~~A~~ An example method for making the scaffold microcarriers porous is ~~a~~ freeze drying in which the bioabsorbable solution is emulsified and frozen, and the solvent subsequently evaporated. There is also a method in which microcarriers are formed from a mixture containing the bioabsorbable material and powdered salt or powdered sugar as a pore forming agent, which is subsequently dissolved and removed to produce porous microcarriers.

Please amend the paragraph beginning on page 54, line 8, as follows:

Because the scaffold microcarriers 1001 are absorbed into the living body and disappear following a predetermined period after injection, surgery to remove the scaffolds after the transplant is unnecessary. Because of this, the load on the patient can be markedly reduced, and, in particular, the load on patients, such as infant and elderly patients, who are lacking in physical strength, can be lightened.

Please amend the sub-heading beginning on page 55, line 12, as follows:

~~Industrial Applicability~~